VOL. XXI. November, 1896. No. 10.

THE

Journal

OF

Nervous and Mental Disease

JOINT MEETING OF THE PATHOLOGICAL SOCIETY OF PHILADELPHIA AND THE PHILADELPHIA NEUROLOGICAL SOCIETY.

Held in Philadelphia May 28, 1896.

Dr. JOHN H. MUSSER, in the chair.

AN INITIAL REPORT FROM THE NEUROLOGICAL LABORATORY OF THE PHILADELPHIA POLYCLINIC.

UNDER THE DIRECTION OF

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The Neurological Laboratory is a part of the Department of Diseases of the Mind and Nervous System in charge of Professors CHARLES K. MILLS and CHARLES W. BURR, who furnish most of the specimens.

LESIONS OF THE BRAIN FOUND IN A CASE OF ACUTE YELLOW ATROPHY OF THE LIVER.

BY CHARLES W. BURR, M.D. AND ALOYSIUS O. J. KELLY, M.D.

THE clinical history of the case is as follows: B. D., male, aged forty years. His previous health had always been good. Having felt poorly for about one month, one week prior to his death he began to complain of chilliness, sweats and vague gastro-intestinal symptoms. His wife then noticed that he was slightly jaundiced. The jaundice rapidly increased in intensity, until before his death it was extreme. On the second day of his illness he began to be delirious and to have general convulsions. The liver dulness became very much decreased in area. The patient vomited often, and his bowels were absolutely constipated. The urine contained leucin and tyrosin, but no albumin. Two days before his death, his delirium passed into stupor, stupor into coma, and in coma he died, Dec. 28, 1895.

The clinical diagnosis was acute yellow atrophy of the liver.

At the necropsy the liver was about one-third the normal size, brown in color, and with wrinkled capsule. It was peculiarly soft to the touch and cut like india rubber. On section the liver structure was indistinctly visible in the right lobe, but absolutely abolished in the left. There was some oozing of bile. The gall bladder contained about an ounce of thick, greenish-black bile, with a little bile sand. There was no obstruction of the ducts, no calculi. The stomach contained a few ounces of bile-stained fluid, but was otherwise normal. The spleen was slightly enlarged and soft. The kidneys were congested, the capsule stripped well; the cortices were well marked off. The brain macroscopically appeared normal.

For the specimens we are much indebted to Dr. L. C. Peter.

The lesions discovered by microscopical examination of the brain may be divided into those found in sections prepared according to the Golgi method and its modifications, and those found in sections stained according to the Nissl methods and modifications. It is convenient to describe the latter first.

Sections from the motor and præfrontal regions of the cerebral cortex after the usual procedures subsequent to hardening in alcohol, were stained with dahlia, vesuvin, magenta red, methylene blue and thionin. While the majority of the stainings with the first mentioned agents were very satisfactory, none of them approached in clearness and sharpness of detail those stained with thionin, according to the method of Lenhossek. The stainings were far superior to those obtained with the much vaunted methylene blue, which latter were, however, better than those obtained with the other dyes. What follows, therefore, refers particularly to thionin preparations, though precisely similar changes were disclosed by the other stainings.

The pathological lesions discovered affect the nucleolus, the nucleus and the cell body (Fig. 1). Normally,

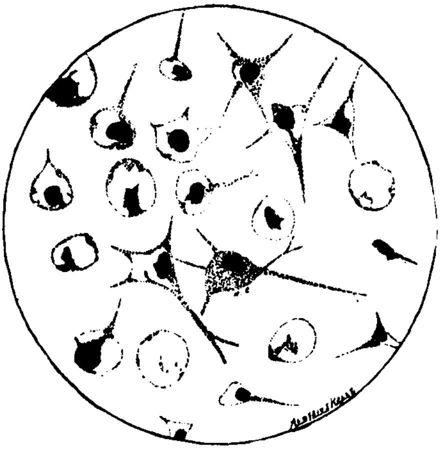

FIG. 1. Drawing illustrating parenchymatous degeneration of the cells of the cerebral cortex; implication of the nucleolus, nucleus, and cell body. The cells in the upper half as in a microscopic field; in the lower half, collected from various regions. N. C., normal cell for comparison. Thionin preparation. x 1200 Zeiss.

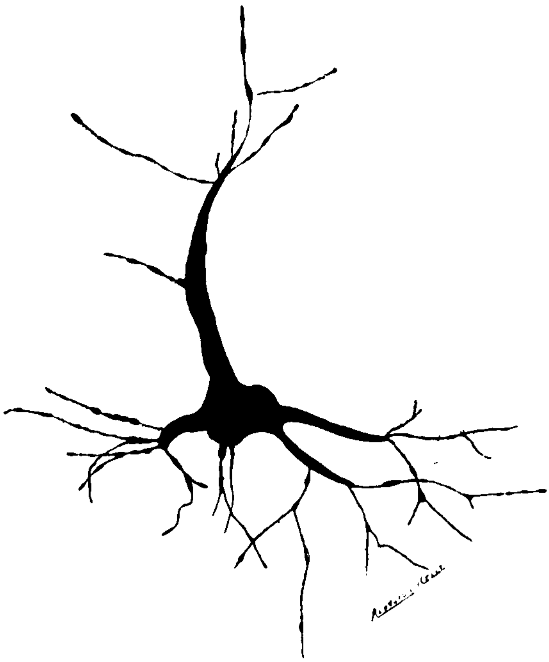

FIG. 2. Drawing illustrating irregular swellings or tumefactions of the dendrites, with loss of the gemmulæ, of a pyramidal cell of the cerebral cortex—early stage of degeneration. Golgi-Berkely preparation.

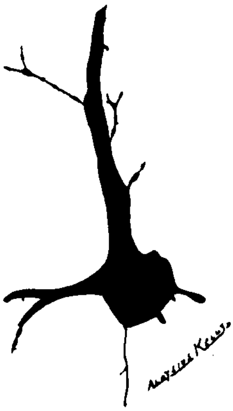

FIG. 3. Drawing illustrating atrophy and disappearance of the dendrites—late stage of degeneration. Golgi-Berkely preparation.

the nucleolus is of a definite size, of rounded contour, with edges smooth and well defined, and has a certain marked, not very variable affinity for the stain. In our preparations the nucleolus is very slightly, if at all, increased in size: it is of somewhat irregular contour, which irregularity is not marked, consisting when demonstrable of a slight and limited projection into the substance of the nucleus at one, occasionally two points, along its periphery; its edges, while sharp and well defined, are not as smooth as normally, and its receptivity of the stain is markedly increased, it appearing as a jet black dot, rendering absolutely futile all attempts to recognize any structure. In its position within the nucleus we can recognize no deviation from the normal, it being situated here and there irregularly as normally.

The nucleus, while apparently exhibiting no marked deviations from the normal variation in size, is frequently distorted in shape, being often elongated, again quite irregular with projections and indentations along various parts of its periphery. The two or three larger and more deeply staining chromophilic particles normally present irregularly arranged within the nuclei, are no longer visible as such. They have lost their identity by reason of the excessive staining which the other finer dust-like chromophilic particles have thus pathologically taken on. The normally clear karyoplasm evinces a decided affinity for the stain, being in many instances excessively stained. This staining of the normally clear karyoplasm and the excessive staining of the nuclear chromophilic particles in many instances, produces such an intense staining of the nucleus as a whole as to obscure the nucleolus, which, in other instances can be quite distinctly recognized.

The cell body seems to be most intensely affected, their being present all gradations from slight implication to almost absolute destruction of it. The chromophilic particles, which normally are distributed throughout the cell body with a certain regularity usually in rows, are in our preparations very irregularly arranged, often showing very curious figures. We notice in some cells but a slight deviation from the normal, the chromophilic particles having disappeared from but a small area, and being possibly more densely aggregated in another region. From this slight change there are visible all gradations of destruction until there remains but the nucleus deeply stained, surrounded by a few particles still stained along the periphery of the cell body. In many instances the chromophilic particles are excessively large. One is inclined to think of a coalescence of smaller ones, as high magnifications (1200) fail to reveal any distinction into parts. In cells manifesting all grades of destructive changes, there is usually arranged around the nucleus a layer of fine, stained dust-like particles, between which and the nucleus, there is always a clear unstained zone.

In some instances the nucleus and cell contents have been entirely destroyed, or the nucleus has dropped out of the cell, and all that is discernable are a few fine stained particles along what was the periphery of the cell. In many cells which are not so excessively affected by the destructive process, there is an appearance extremely suggestive of fat globules and detritus. The fat therefrom may unfortunately have been removed during the process of hardening.

The protoplasmic processes as far as they are stained present in some instances changes similar to those described as affecting the cell body. In most instances, however, they exhibit no deviation from the normal.

The pathological changes described affect all varieties of cortical cells. We have been unable to discover that any one variety is more affected than another. In spots, however, the destructive process has been more marked than elsewhere. In certain regions all the cells in a quite considerable area are more or less destroyed, while in others but few cells are implicated. This applies to all the layers of cortical cells. Again, in a few places it seems as though the more superficial cells were more intensely affected than those of the deeper layers. These instances, however, are very few.

Other pieces of cortex after hardening in Müller's fluid were stained according to the silver phosphomolybdate method of Berkely. The difficulty of determining, by this and the ordinary Golgi method of staining, the number of cells affected is very great owing to the uncertainty of the impregnation and to the fact that of all the cells of the various layers of the cortex but a very few are at any one time stained. This latter fact is, however, a great advantage, as we are thereby enabled to study much more readily the changes affecting the individual cells and their prolongations. This method of staining is inappropriate for detecting the finer changes in the cell body, and in our preparations gave negative results. The changes affecting the prolongations are, however, quite definite. They are of two kinds, or, as we prefer to say, two stages of one process. The first consists of a swelling (Fig. 2), the second of an atrophy of the processes (Fig. 3).

The first are more numerous. They consist of irregular swellings or tumefactions which extend along the dendrites for a variable distance, and are of variable thickness. Some are very minute, others quite large. The apical process itself is very frequently affected close to the cell body proper. In other instances the parent dendrite and its finer branches abruptly become thickened, and as abruptly resume their normal calibre. As a rule, throughout the course of these tumefactions the gemmulæ are absent, though occasionally one still detects a few projecting from the periphery of the swellings. Along some of the finer dendrites not the subject of such pathological tumefactions, the gemmulæ have also disappeared. In other instances they themselves appear somewhat swollen. The varicosities normally present at the point of branching of the dendrites appear in many instances to be excessively large.

The further stage of this destructive process has already been alluded to as an apparent atrophy. The gemmulæ have entirely disappeared from the dendrites—a very few may occasionally still persist. The dendrites themselves have become thinned and shortened. That they have not been broken or cut off during the process of preparation, is evident from the fact that at their distal extremities they appear rounded and well defined. Further, many of the dendrites have entirely disappeared. In some of these latter instances, as well as in some of the former, the apical process is still quite thick.

This destructive process affects apparently indiscriminately the various cells of the several layers of the cerebral cortex. The determination of the number of the implicated cells is, however, as before stated, impossible. We could detect no pathological changes in the axis-cylinders or collaterals.

The study of the cerebellum led to very indefinite results. Aside from variations in the intensity of the staining of the Purkinje cells, nothing of any note was discovered by the use of the aniline dyes. The impregnation of the cells of the cerebellum by the Berkely modification of the Golgi method was less satisfactory than was that of the cells of the cerebrum, but the alterations found in the Purkinje cells were practically the same as those described affecting the cells of the cerebral cortex. We detected no change in the neuroglia elements of either the cerebrum or cerebellum, and no disease of the blood-vessel walls.

To sum up we have found evidences of a marked destructive process affecting the bodies and the processes of the nerve cells of the cerebral cortex. The lesion is parenchymatous affecting the nerve cells primarily, and is not secondary to any disease of the blood vessels. We are entirely ignorant of the primary cause of this destructive process. It is more than probable, it is almost certain, that acute yellow atrophy of the liver is caused by a poison, and that it is not a local but a general constitutional disease, a toxemia. And since cerebral symptoms, delirium, perhaps mania, general or local convulsions and coma form no small part of its clinical history, we should expect to find distinct signs of disease in the cortex whether such signs be the result of penetrated function or its cause. The fact that heretofore microscopic study of the brain in conditions of delirium, acute mania, and the acute infectious fevers has frequently been fruitless or indefinite, proves nothing, since we are only now beginning to learn methods of research competent to show any of the finer microscopic changes. As methods have improved, the number of so-called functional diseases has steadily decreased. Granting that acute yellow atrophy of the liver is a toxemia we are confronted with the question as to whether the brain lesions found are due to the same poison or whether they are due to another or to others produced by disturbance of any of the body functions. We cannot answer it. We have, of course, assumed that the lesions found by us in this one case are not accidental, but essential.

Whether this be so can only be proven by the study of other cases. The lesions found are, of course, not claimed to be characteristic of acute yellow atrophy of the liver. Indeed, we should expect to find similar changes in the acute infectious fevers accompanied by similar brain symptoms. As a matter of fact the lesions found in this case by using Berkely's modification of Golgi's method correspond to those found experimentally by Berkely in ricin and alcohol poisoning and are not unlike those described by Andriezen and others as occurring in certain types of insanity, notably alcoholic dementia.

That the case was one of acute yellow atrophy of the liver is proven not only by the clinical history and the necropsy, but also by the microscopical examination of the liver, spleen and kidneys.